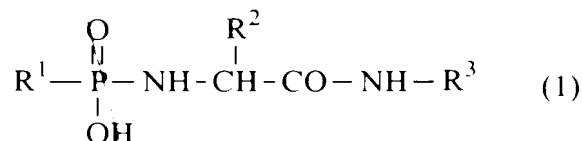


phosphonic acid derivatives having the following formula (1):

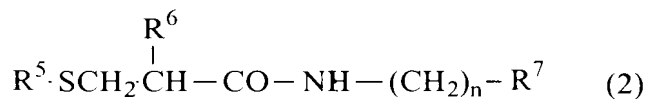


wherein R<sup>1</sup> is a hydrogen atom, a hydroxyl group, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted,

R<sup>2</sup> is a hydrogen atom, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted, and ,

R<sup>3</sup> is a hydrogen atom or a -CH(R<sup>4</sup>)COOH in which R<sup>4</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and salts thereof; and

mercaptopropionamide derivatives having the following formula (2):



wherein R<sup>5</sup> is a hydrogen atom or an acyl group, R<sup>6</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and

R<sup>7</sup> is a hydrogen atom, a carboxyl group, an alkoxycarbonyl group, a hydrocarbon group which may be substituted, a heterocyclic group which may be substituted, or an acyl group, and n is a number of 1 to 20.--

#### SUPPORT FOR THE AMENDMENT

Support for the amendment to Claim 1 is found in Claim 2 as originally filed.

Support for the amendment to claim 7 is found on page 5, line 6 of the specification. No new

matter would be added to this application by entry of this amendment. A marked-up copy of the claims, as amended, is attached.

Upon entry of this amendment Claims 1, 3-4 and 6-21 will now be active in this application.

#### REQUEST FOR RECONSIDERATION

Hair growth in mammals, and especially humans provides many opportunities for modification of appearance. Many efforts are undertaken to promote the growth of hair in particular areas as well as to remove or prevent the growth of hair in other areas. While primarily a cosmetic matter, the development of hair growth in regions where such growth is not desired can be troublesome. Some methods for removing hair from unwanted areas have here to fore been difficult and/or uncomfortable. Accordingly, new methods of reducing hair growth are sought.

The present invention addresses this problem by providing a method of inhibiting hair growth, by topically applying to an affected area **inhibitors of elastase-like enzymes or neutral endopeptidase, which are not inhibitors of matrix metalloproteinase (MMP)**. Applicants have discovered that inhibition of these enzyme activities can result in the reduction of hair growth in the treated area. Such a method is nowhere disclosed or suggested in the cited prior art of record.

The rejection to Claim 2 under 35 U.S.C. §112, first paragraph, is respectfully traversed.

Proteinases are classified into four groups, metalloproteinases, serine proteinases, carboxyl proteinases and thiol proteinases. Matrix metalloproteinase (MMP) is only one of a

class of enzymes belong to metalloproteinases. In this area of technology, the term "inhibitors of metalloproteinase" means an agent which inhibits all enzymes belonging to metalloproteinase. However, inhibitors of MMP, are not ones which can inhibit all the enzymes belonging to the metalloproteinase group, even though MMP belongs to metalloproteinases. Similarly inhibitors of elastase-like enzymes or neutral endopeptidase, are not ones which can inhibit all the enzymes belonging to the metalloproteinase group even though elastase-like enzymes or neutral endopeptidase belongs to the genus of metalloproteinases. Therefore, inhibitors of MMP dose not mean inhibitors of the entire genus of metalloproteinase, such as elastase-like enzymes or neutral endopeptidase. Inhibitors of the entire genus of metalloproteinases are not described in Tsuji et al. Since the genus of metalloproteinase is broader than the species of matrix metalloproteinase, and also includes elastase-like enzymes and neutral endopeptidase, inhibitors for elastase-like enzymes and neutral endopeptidase enzymes which are not inhibitors of matrix metalloproteinase is enabled to those of ordinary skill in the art without undue experimentation.

Moreover, the burden is on the Patent Office to provide reasons and/or examples to doubt the objective enablement of the claimed invention, a burden which has not been met by the Examiner. Applicant's disclosure must be taken as in compliance with the enabling requirement under 35 USC 112, first paragraph, unless, there is reason to doubt the objective truth of the statements contained therein. (In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971)). The disclosure of Tsuji et al. does not provide sufficient basis to doubt the objective enablement of the claimed invention. For these reasons, withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

The rejections of Claims 1-4 under 35 U.S.C. §102(e) over Styczynski et al and of Claims 1-4 and 6-21 under 35 U.S.C. §102(a) over Tsuji et al are respectfully traversed.

None of the cited prior art of record discloses or suggests that hair growth can be inhibited by topical administration of **inhibitors of elastase-like enzymes or neutral endopeptidase, which are not** "matrix metalloproteinase"(MMP) inhibitors.

Styczynski et al discloses a method of reducing hair growth using inhibitors of matrix metalloproteinases (MMP). Inhibitory activity for no other enzyme is suggested by this reference.

In contrast, the present invention is directed to a method of inhibiting hair growth, in which inhibitors of elastase-like enzymes or neutral endopeptidase inhibitors are administered, such enzymes not belonging to matrix metalloproteinase (MMP). Applicants note that the claims have been amended to recite that the claimed method uses **inhibitors of elastase-like enzymes or neutral endopeptidase, which are not matrix metalloproteinase (MMP) inhibitors**. Applicants further note that this limitation is an existing limitation of claim 2 as originally presented. Accordingly, Applicants' amendment is not a narrowing of the claimed subject matter of claim 2 and there interpretation of the this claim element under the Doctrine of Equivalents should not be precluded (*Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co. Ltd.* (Fed. Cir. 2000)).

The cited prior art reference only discloses the use of a matrix metalloproteinase (MMP) inhibitor for the inhibition of hair growth. There is no suggestion to administer a compound against enzymes other than matrix metalloproteinase (MMP). Matrix metalloproteinase (MMP) is explicitly excluded by the present claims. Since there is no suggestion in the prior art of record to administer inhibitors of elastase-like enzymes or

neutral endopeptidase, which are not matrix metalloproteinase inhibitors, the claimed invention is clearly neither anticipated nor obvious from this reference and accordingly the withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Tsuji et al is directed to a method of preventing wrinkles and not a method of inhibiting hair growth. Applicants respectfully submit that there is no motivation to apply the compounds of Tsuji et al **to an affected area of a subject in need of hair growth inhibition**, as there is no suggestion in the cited reference of the activity of hair growth inhibition. Again, the reference is directed to a method of preventing wrinkles, a phenomena to which the record provides no causal relationship. For this reason, since there is no suggestion of hair growth inhibition by the administration of the compounds of Tsuji et al, the claimed method is clearly neither anticipated nor obvious from this reference and accordingly withdrawal of the rejection under 35 U.S.C. §102(a) is respectfully requested.

Applicants note that the claims specifically recite that **the method** is directed to a method in which the compounds are topically administered **to an affected area** of the subject in need thereof. Accordingly, any effects found in the prior art by using the disclosed compounds for the prevention of wrinkles, do not anticipate nor make obvious a method of inhibiting hair growth.

The rejection of Claims 7-21 under 35 U.S.C. §112, second paragraph, has been obviated by appropriate amendment.

Applicants has now amended Claim 7 to recite "phosphonic acid derivatives" as suggested by the Examiner. However, since the structure of Formula (1) is provided in the claims, such amendment is not necessary as those of ordinary skill in the art would be able to determine whether or not a specific compound fell within the scope of Formula (1), in the

absence of the specific nomenclature used. In view of Applicants' amendment and arguments, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

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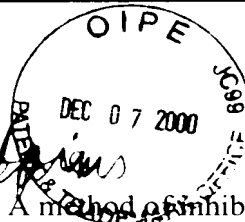
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Serial No:	011-23,611
Amendment Filed on:	DEC. 7, 2000

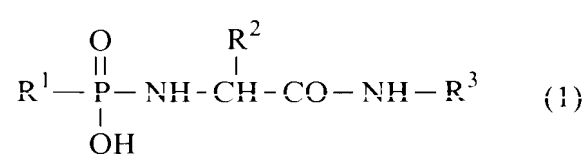
--1. (Twice Amended) A method of inhibiting hair growth, which comprises topically administering to an affected area of a subject in need thereof an inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor, wherein said inhibitor of elastase-like enzymes are not a matrix metalloproteinase inhibitor.

7. The method according to Claim 1, wherein said inhibitor of elastase-like enzymes or a neutral endopeptidase inhibitor is selected from the group consisting of:

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[phosphoric] phosphonic acid derivatives having the following formula (1):

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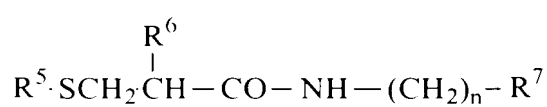


wherein R<sup>1</sup> is a hydrogen atom, a hydroxyl group, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted,

R<sup>2</sup> is a hydrogen atom, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted, and

R<sup>3</sup> is a hydrogen atom or a -CH(R<sup>4</sup>)COOH in which R<sup>4</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and salts thereof; and

mercaptopropionamide derivatives having the following formula (2):



wherein R<sup>5</sup> is a hydrogen atom or an acyl group, R<sup>6</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and



$R^7$  is a hydrogen atom, a carboxyl group, an alkoxycarbonyl group, a hydrocarbon group which may be substituted, a heterocyclic group which may be substituted, or an acyl group, and  $n$  is a number of 1 to 20.